Biomathematics: From Daphnia to Dengue

**[1]Koh Hock Lye, [2]Lee Hooi Ling, Teh Su Yean,
Saw See Keong and Ahmad Izani Md Ismail**
[1]*School of Mathematical Sciences
Universiti Sains Malaysia, 11800 Penang, Malaysia*
[2]*Technip GeoProduction Malaysia*

ABSTRACT

The study of biological and ecological systems by means of mathematical models and computer simulations has gained popularity and wide acceptance. A major impetus towards this development could be traced to the rapid advances in computer hardware and software that enables the study of large ecosystems with adequate resolution and makes possible the inclusion of refined details. The fundamental mathematical theory has also evolved significantly to support these computations. In this invited talk, we will briefly present an exposition of mathematical simulations of ecosystems subject to environmental stress such as temperature, hydro period, dissolved oxygen and toxicants to assess the impact on ecosystem health. The ecosystems concerned include daphnia, mussels, fish and mosquitoes. Daphnia is a key organism in the food chain; hence, any disturbance to the ecosystems of daphnia will have extensive impacts over the entire trophic levels above daphnia. Mussels have served as an indicator organism to reflect the degree of aquatic pollution and its impacts on the aquatic ecosystems. Fish is a major source of protein. Contamination of fish by toxicants such as PCBs and mercury has immediate implications to fish population dynamics and human health. Insights gained from aquatic ecosystem modeling and simulation provided useful concepts and approaches to mathematical simulations of the distribution of Aedes *aegypti*, a species of mosquito that transmit dengue fever. The main objective of this presentation is to demonstrate that mathematical modeling and simulations can be effectively used to study biological and ecological systems.

Key words: Biomathematics, ecological models, dengue, daphnia, mussels, fish

INTRODUCTION

A classic approach to the analysis of population dynamics consisted of a system of differential equations whose solutions were perceived to reflect the dynamics of the state variables involved, an example of which is the Lotka-Volterra models or the logistic model (Murray, 1993). This set of differential equations can be studied by utilizing analytical as well as numerical approaches. However, this approach has been perceived to have limitations in that over simplification of the life history of the organisms (state variables) may render the conclusions derived from this approach

somewhat unrealistic. To preserve as much realism as possible, life history characteristics of individual organisms must be realistically represented in the models. This dictates a slightly different approach to ecosystem modeling, in which individual responses that incorporate refined life history characteristics are integrated into population dynamics.

In this paper, we will briefly present an exposition of mathematical simulations of ecosystems subject to environmental stress such as temperature, hydro period, dissolved oxygen and toxicants to assess the impact on ecosystem health. The ecosystems concerned include daphnia, mussels, fish and mosquitoes. Daphnia is a key organism in the food chain; hence, any disturbance to the ecosystems of daphnia will have extensive impacts over the entire trophic levels above daphnia. Mussels have served as an indicator organism to reflect the degree of aquatic pollution and its impacts on the aquatic ecosystems. Fish is a major source of protein. Contamination of fish by toxicants such as PCBs and mercury has immediate implications to fish population dynamics and human health. Insights gained from aquatic ecosystem modeling and simulation provided useful concepts and approaches to mathematical simulations of the distribution of Aedes *aegypti*, a species of mosquito that transmit dengue fever. The main objective of this presentation is to demonstrate that mathematical modeling and simulations can be effectively used to study biological and ecological systems. To preserve as much realism as possible, our models will incorporate life history of the organisms as much as possible, as will be demonstrated in the following sections.

Individual-based Model for Daphnia

To enhance the realism of mathematical models, an approach known as individual-based model (IBM) has been proposed, in which details of individual organisms with realistic life history parameters are incorporated into the population model. For example, in modeling daphnia population subject to the combined effects of environmental and chemical stresses, the IBM approach is used to describe the detailed life history of an individual daphnia (Figure 1). This approach incorporates process parameters obtained from extensive literature review of daphnia physiology and ecology (Figure 2). In this model an individual daphnia grows and if the environment is suitable, it reproduces at regular intervals. Environmental conditions such as toxicity, resources, temperature and dissolved oxygen (DO) collectively determine the respiration rate and filtering rate, which in turn will influence the growth and fecundity of daphnia. The individual models incorporating these biological details are then integrated into a population model by an extended McKendrick-von Foerster equation (Equation 1). The main

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purpose of this type of models is to investigate the effects observed in the population dynamics that are caused by impacts on physiology of individuals (Koh et al., 1997). The population ρ is represented by Equation 1, which is a hyperbolic partial differential equation that describes the population in terms of a density function $\rho = \rho(t, a, m_L, m_S)$, measured in terms of numbers per age per lipid mass, per structure mass, per volume of the environment.

$$\rho_t + \rho_a + (\rho_{g_L})m_L + (\rho.g_S)m_S = -\mu\rho \tag{1}$$

The term μ represent non-linear mortality due to density, toxicity and low DO. The boundary condition consists of a birth process represented by

$$\rho(t,0,m_{L_0},m_{S_0}) = \int \beta(t,a,m_{L_0},m_{S_0},m_L,m_S) \times \rho(t,s,m_L,m_S) \, da \, dm_L \, dm_S. \tag{2}$$

This population model, which is based upon detailed individual physiology, can then be used to determine indicators of stress at the population level due to the combined effects of environmental and chemical stresses on individuals. A striking insight that arises from this type of analysis is that population effects can be far more damaging than what can be expected from known level of effects on the individuals; and that the combined effects of environmental and chemical stress can considerably reduce the parameter ranges indicative of population survival as compared to the effects of the single stresses, with far reaching implication (Koh et al., 1997). For example, during the summer months, the discharge of heated cooling water into rivers can typically raise the ambient thermal regime by 8 to 9 °C. It is known that higher temperature typically reduces level of DO in the aquatic environment, which in turn serves to exert additional stress on daphnia physiology. Elevated toxicity usually associated with industrial activities may then deliver a final blow to daphnia population that subsists near extinction, an observation that is typically produced in our simulation exercises and repeatedly encountered in the field. To replicate in the laboratory these observations derived from model simulations over an extended period of time would require resources that are far beyond the reach of most laboratories. We are unaware of laboratory experiments that investigate the combined interactive impact of chemical toxicity, thermal and oxygen stresses on the population survival of daphnia. Simulation models appear to be the only viable alternative for the time being.

Modeling Fish Ecology

Fish communities are regularly exposed to a large number of natural and synthetic toxic chemicals, whose harmful effects, both short term and long term, need to be studied. A time-concentration-effect model has been developed to assess the long-term effect of PCBs on multi generations of fish communities in the Florida Everglades (Al-Rabai'ah et al., 2005). The term "fish" is used here generically to refer to five functional fish groups (FGs), two having small and two having large adult size and the crustacean (crayfish), each of which are further composed of several age classes. Age and size structure is recognized as important attributes in ecosystem studies; hence it is incorporated in the model. The model predicts the *population* response time series for each FG based upon toxicant (PCB) exposure concentration and duration (Table 1 and 2). Figure 3 shows the density of FG 2 (livebearer), over a period of 5000 days for four scenarios of toxicity. The annual fluctuation in fish density simulated is induced by an incorporation of hydro period, temperature and toxicity on the Everglades fish ecology (Koh et al., 2004). Model results indicate that a concentration of 0.1 μg/L begins to have adverse effects on survival and reproduction success for the Everglades fish communities. For comparison, the USEPA (United States Environmental Protection Agency) has stipulated a standard of 0.014 μg/L for the protection of freshwater fish from chronic effects and a standard of 1.0 μg/L from acute effects. Lethal Concentration LC or Effect Concentration EC is normally determined in the laboratory over short duration (4 to 14 days for example) covering less than one generation. To determine the toxicity effects on fish populations over multi generations by laboratory experiments covering thousands of days would demand exorbitant resources far exceeding what could normally be made available. However, appropriate model simulations could readily overcome this deficiency. The efficiency of model simulations to complement laboratory studies is amply demonstrated in this model approach.
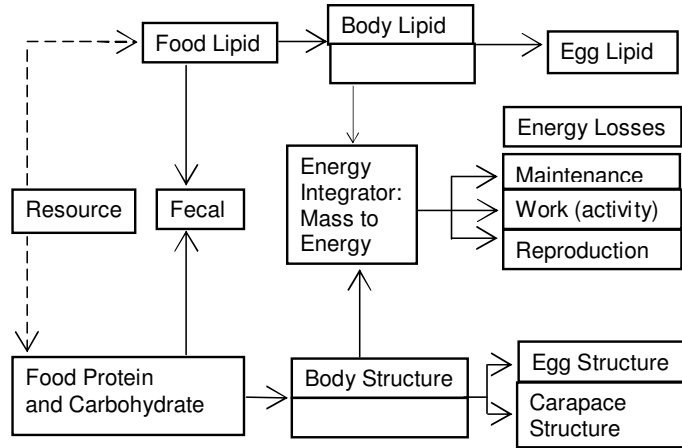
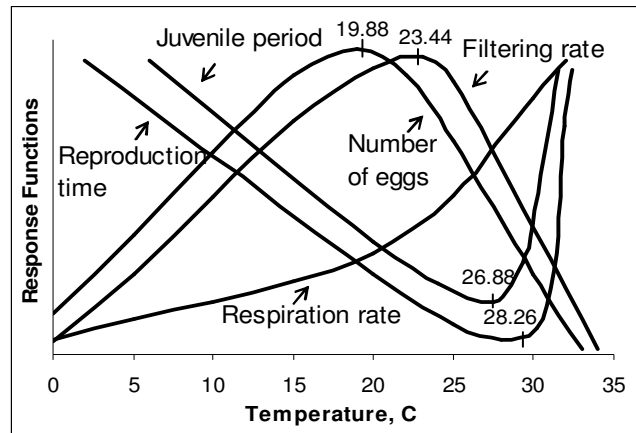Figure 1: Compartment and flow diagram for an individual daphnid

Figure 2: Daphnia temperature response functions

TABLE 1: Some mortality toxicity values for the Everglades FGs

Endpoint (µg/L)	Killifish (FG 1)	Livebearer (FG 2)	Sunfish (FG 3)	Crayfish (FG 4)	Florida Gar (FG 5)
4-day LC$_{50}$	148	256	326	213	462
14-day LC$_{50}$	68	101	107	89	145

TABLE 2: Some hatchability toxicity values for the Everglades FGs

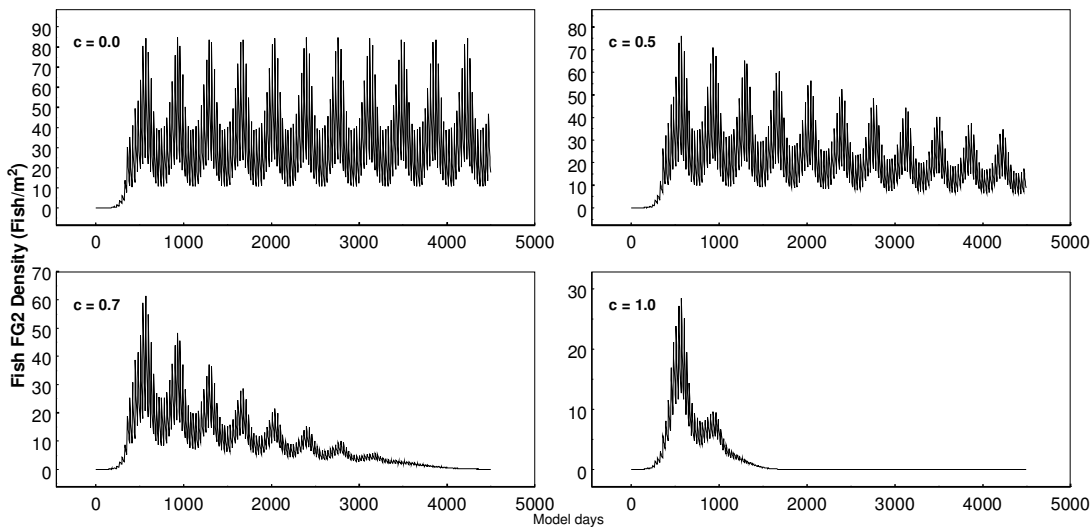| Endpoint (µg/L)	Killifish	Livebearer	Sunfish	Crayfish	Florida Gar
4-day EC$_{50}$	141.61	258.39	337.47	211.49	495.08
14-day EC$_{50}$	60.14	92.87	99.31	80.92	137.93

Figure 3: Model prediction of population density for FG 2 in response to PCB concentration c (µg/L)

Proposed Models for Dengue

The dengue disease exhibits only one epidemiological cycle linking the human host and the A. *aegypti* vector. A susceptible female A. *aegypti* is infected by sucking infected human blood, after which it undergoes a short incubation period of approximately eight days. Subsequently, the virus begins a replication process inside the mosquito's salivary glands and the mosquito is ready to infect susceptible humans. When an infected mosquito bites a susceptible human, the virus is injected into his/her blood stream and begins an incubation period, which takes from three to ten days, with an average of five days. Following this, a dengue may evolve to a non-symptomatic stage or to a classic set of symptoms. Symptoms persist for a period of three to seven days, during which the human is infective. Upon recovery, the individual develops a specific immunity for a long time (Gubler, 1998). In some cases, a serious symptom shows up, called 'dengue haemorrhagic fever', characterized by coagulation problems, which may lead to death.

It is well known that mosquitoes spread and invade in the form of wave fronts (Vasconcelos et al., 1999), similar to the ways others adopted to spread and colonize, including mussels (Lee and DeAngelis, 1997) and cancer cells (Gatenby et al., 1996; Perumpanani et al., 1996; Byrne et al., 1999). Numerical simulations can be performed to estimate and relate the wave front speeds, with which the mosquitoes spread, to a few crucial environmental and biological parameters. Strategies for mosquito invasion containment and the prediction of the impact can be analyzed and proposed,

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based upon model simulations incorporating relevant measurable parameters that influence A. *aegypti* population dynamics. Various simulation models developed to devise strategies for controlling the propagation of mussel communities (Lee et al., 1998), for managing daphnia population (Koh et al., 1997) and the Everglades fish communities (Koh et al., 2003, 2004; Al-Rabai'ah et al., 2002, 2005) can be adapted for mosquitoes.

Without the prospect of an effective and cheap vaccine in the near future, any feasible public policy for controlling dengue epidemics in tropical climates must necessarily include appropriate strategies for minimizing the mosquito population, e.g. application of chemicals to kill mosquitoes and their larvae or by the eradication of their breeding grounds. Mathematical models will be developed to simulate A. *aegypti* population dispersal dynamics, with the ultimate aim to devise practical procedures for the effective minimization of A. *aegypti* population so as to reduce its impact as a dengue vector. Models that can be developed include reaction-diffusion models that incorporate the life cycle of A. *aegypti* and climatic-environmental parameters such as rain and temperature that influence the population dynamics of A. *aegypti*. These models will establish a solid and tractable knowledge of the A. *aegypti* population dynamics in order to find control parameters appropriate for the eradication of A. *aegypti* by practical intervention. Questions of how mosquitoes respond to physical, chemical and environmental conditions to produce spatial temporal patterns of distributions can be answered. A sound understanding of this distribution patterns through mathematical modeling will provide additional information on the best approaches to eradicate the hazards of A. *aegypti*.

Mathematical models can provide such knowledge as well as yield the desired control parameters. In a recent paper, Abramson et al. (2003) analyzed traveling waves in a one-dimensional model that incorporates a diffusion process and non-linear growth for the Hantavirus infection in deer mice in the American Southwest. The interaction of the non-linear growth with diffusion provides a mechanism for the formation of stable traveling waves in the form of fronts. The existence of dynamical phenomena such as these traveling fronts opens the interesting possibilities of subjecting a model prediction to experimental verification. The observation of this in real mice population provides a valuable source of data to assign realistic values to the parameters of the mathematical models. This approach should be applicable to the dengue epidemic models. It is well known that mosquitoes disperse in the form of traveling waves (Murray et al., 1986; Murray, 1993; Cummings et al., 2004), with characteristics that can be determined from the simulation models. Numerical simulations can be performed to estimate the wave front velocity and other characteristics as functions of some of the

biological and environmental parameters. Winged female A. *aegypti* in search of human blood or places for oviposition are the main media for local population dispersal. The limited range of flight accounts for the local advance of a mosquito infestation. On the other hand, wind currents may result in a rapid long-range movement of large masses of mosquitoes and consequently may cause a quick advance of infestation (Takahashi et al., 2005). An appropriate approach should initially focus its attention on a small spatial scale, in which a local diffusion process due to autonomous and random search movements of winged A. *aegypti* is responsible for the dispersal. This local scale of diffusion will be coupled to advection, typically interpreted as the result of wind and human transportation, to form a diffusion-advection equation to model the dispersal of winged mosquitoes within small spatial domains. Considering the vital dynamics and dispersal process together, an eight-parameter mathematical model (Equation 3) may be formulated by using two coupled conservation laws, where M is the winged mosquitoes and A is the aquatic forms, similar to the form used by Abramson et al. (2003).

$$\frac{\partial}{\partial t}M(x,t) = D\frac{\partial^2}{\partial x^2}M(x,t) - \frac{\partial}{\partial x}\big(vM(x,t)\big) + \gamma A(x,t)\left(1 - \frac{M(x,t)}{k_1}\right) - \mu_1 M(x,t)$$

$$\frac{\partial}{\partial t}A(x,t) = r\left(1 - \frac{A(x,t)}{k_2}\right)M(x,t) - (\mu_2 + \gamma)A(x,t).$$

$$(3)$$

CONCLUSION

Mathematical and computer simulation (numerical models) have made possible vast improvement in our understanding of biological and ecological systems. Numerical models have advantages over laboratory models in that numerical models are cost-effective, flexible and portable. Numerical models have certain advantages over laboratory or field experiments for testing ecological hypothesis over a very long time period, as they are superior in investigating phenomena governed by a wide range of parameter values. In this paper, we have demonstrated the efficiency of numerical models for simulating daphnia and fish ecology and outlined an approach for modeling dengue, based upon adaptation of methodology used in previous studies.

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